

Risk factors of hypotension during cesarean section with spinal anesthesia in parturients with COVID-19: a retrospective study in comparison with pregnant women without COVID-19

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Background: The incidence of hypotension in parturients with coronavirus disease (COVID-19) undergoing regional anesthesia remains controversial. This study aimed to investigate the incidence of hypotension during spinal anesthesia in parturients infected with COVID-19, as well as to identify associated risk factors.

Methods: This retrospective study compared COVID-19-positive parturients who underwent cesarean section under spinal anesthesia (COVID-19 group) with a control group between January 2017 and June 2022. We reviewed the medical records and collected the following information: basic patient characteristics, spinal anesthesia, and newborn-related data.

Results: Compared with the control group, the COVID-19 group did not show any significant differences in terms of hypotension occurrence and vasopressor usage. A positive correlation was noted in the COVID-19 group between heart rate and duration of hospital stay ($P < 0.001$, Spearman's $\rho = 0.422$). In subgroup analysis of the COVID-19 group, group with a baseline heart rate ≥ 100 (group H) had lower Apgar scores at 1 min, longer hospital stays, and more severe COVID-19 symptoms than the with a baseline heart rate < 100 (group L). Moreover, in group H, there was a positive correlation between the heart rate and the lowest systolic blood pressure after spinal anesthesia ($P = 0.012$, Spearman's $\rho = 0.528$).

Conclusions: Parturients with COVID-19 do not appear to have a higher risk of hypotension during cesarean section under spinal anesthesia than those without COVID-19. Given the close association between preoperative heart rate and extent of hypotension in parturients with COVID-19 undergoing spinal anesthesia, vigilant monitoring of vital signs by anesthesiologists is crucial during the perioperative period.

Keywords: COVID-19; Hypotension; Pregnancy; Risk factors; Spinal anesthesia; Tachycardia.

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INTRODUCTION

The global pandemic of the SARS-CoV-2 virus, coronavirus disease 2019 (COVID-19), which began in 2019, has been

ongoing for almost 5 years. The virus continues to spread worldwide with multiple variants emerging and maintaining high levels of infectivity. Fortunately, vaccines and treatments have been developed during this pandemic. However,

uncertainty remains regarding the end of the pandemic.

Along with the progression of the pandemic, various medical issues that were not well known in the early stages of the outbreak have gradually been uncovered. One of these issues is the occurrence of hypotension during epidural anesthesia in parturients infected with COVID-19. However, the exact reason for this remains unclear. However, there is an opinion attributing this to autonomic dysfunction, which is frequently observed in patients infected with the COVID-19 virus or those who have received vaccinations for prevention [1-3]. Another argument suggests that this may be related to the binding of the COVID-19 virus to the angiotensin-converting enzyme-2 receptor, which plays a crucial role in blood pressure regulation [4].

However, most studies published to date on epidural anesthesia in parturients with COVID-19 have been small-scale studies or have involved the combined use of epidural and spinal anesthesia [5-8]. In particular, comparing epidural and spinal anesthesia on the same basis is not appropriate, as they differ in terms of the anesthesia method, drug concentrations, and dosage.

Since 2020, our institution has served as a dedicated hospital for patients with COVID-19 in South Korea. We have conducted numerous cesarean sections in parturients with COVID-19. Almost all parturients with COVID-19 who underwent a cesarean section received spinal anesthesia, with general anesthesia administered only when spinal anesthesia was not feasible. Many anesthesiologists from our institution who participated in these surgeries expressed the opinion that there appears to be an increased incidence of hypotension and elevated heart rate during spinal anesthesia in parturients with COVID-19 compared to that in general obstetric patients. In response to this observation, the authors conducted this study to investigate whether parturients with COVID-19 experience hypotension and an increase in heart rate during spinal anesthesia compared to general parturients.

The primary endpoint of our study was the occurrence of hypotension during spinal anesthesia in parturients with COVID-19. Additionally, we investigated the perioperative factors that may influence them.

MATERIALS AND METHODS

The retrospective study was approved by the research board (Institutional Review Board) of our institution under the protocol number nmc-2022-09-099. We retrospectively

reviewed medical records of adult female aged 18 years and above who underwent cesarean delivery with spinal anesthesia at our institution from January 2017 to August 2022.

The inclusion criteria were adults aged 18–64 years with an American Society of Anesthesiologists physical status class I–II. Patients who were taking medications that could affect the heart rate or who had cardiovascular diseases were excluded from the study.

The patients were divided into two groups: the COVID-19 group, which included those confirmed to have COVID-19 who underwent cesarean section during the isolation period, and the control group, consisting of non-infected parturients who underwent cesarean section. The control group was statistically matched for age, weight, and height with the COVID-19 group.

Within the COVID-19 group, a subgroup analysis was conducted by dividing the heart rate into a group with a heart rate > 100 beats/min (group H) and a group with a heart rate of less than 100 beats/min (group L). The Apgar score, newborn body weight, duration of postoperative hospital stay, and worsening of COVID-19 symptoms were compared between the two groups. Worsening COVID-19 symptoms were defined as increased oxygen demand, C-reactive protein (CRP), and procalcitonin levels.

Basic patient characteristics, such as age, height, post-pregnancy weight, body mass index (BMI), American Society of Anesthesiologists class, gestational age, fasting status before surgery, preoperative baseline heart rate (BHR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and urgency of surgery, were recorded. Additionally, COVID-19-related factors, including the date of COVID-19 confirmation and the degree of respiratory symptoms related to COVID-19, were documented, which were categorized as none, mild (fever, dyspnea, no oxygen administered), moderate (nasal O₂ cannula applied), or severe (O₂ mask applied).

For spinal anesthesia, the dosage of bupivacaine and fentanyl used, needle insertion method, needle insertion site, sensory nerve block level, baseline oxygen saturation (SpO₂), BHR, SBP, and DBP were recorded immediately upon arrival in the operating room, lowest blood pressure during spinal anesthesia, amount of phenylephrine and ephedrine used during anesthesia, amount of colloid and crystalloid used during anesthesia, time from spinal anesthesia to incision, and total surgical time. Newborn-related parameters, including newborn weight and Apgar scores at 1 and 5 min, were also documented.

If any of the data items listed above were missing, they were excluded from analysis.

None of the patients received any premedication. Non-invasive blood pressure measurement, electrocardiography, pulse oximetry, and capnography were used for intraoperative monitoring. After measuring baseline vital signs, all patients received 5 L/min of oxygen via a simple mask. Spinal anesthesia was administered using 0.5% bupivacaine and fentanyl. The dosage of bupivacaine was determined at the discretion of the anesthesiologist, and a standard dosage of 10 µg of fentanyl was administered to all patients. The procedural position for spinal anesthesia was the left lateral decubitus position for all patients, with needle insertion performed midline or paramedian, and the needle insertion site located in the lumbar spine at the L3–4 or L4–5 space. Immediately after the injection, the patient was placed in the supine position. Sensory nerve block level assessment was performed 2 min after drug injection.

During surgery, phenylephrine or ephedrine was administered if the SBP dropped below 90 mmHg, if there was a reduction of 20% or more from baseline SBP, or based on the anesthesiologist's judgment. Additionally, the amount of colloid or crystalloid infused was adjusted during surgery based on the amount of blood loss and the volume depletion status of the patient.

Postoperatively, the patient with COVID-19 was managed according to the hospital's infection control guidelines. The patient was transferred to the isolation operating room, where a simple mask was applied for 30 min at a rate of 5 L/min, followed by monitoring of vital signs. Subsequently, the patient was transferred to the infection isolation ward. Non-infected patients were moved to the recovery room after surgery, where they underwent 30 min of vital sign monitoring before being transferred to their regular hospital room.

Statistical analysis

Statistical analyses were performed using SPSS Statistics (version 25.0, SPSS Inc.). Variables with a normal distribution were expressed as the mean (standard deviation), while those with a non-normal distribution were represented by the median (25–75% percentile). Between-group comparisons for continuous variables were conducted using Student's unpaired *t*-test or the Mann-Whitney *U* test, and for categorical variables, the chi-square test was applied. The relationship between BHR and length of hospital stay, as

well as the relationship between BHR and the lowest blood pressure after spinal anesthesia, were analyzed using Partial Spearman correlation analysis and multiple logistic regression. Statistical significance was set at $P < 0.05$.

RESULTS

The COVID-19 group comprised of 83 parturients from January 2021 to June 2022. After excluding 4 parturients who were in self-quarantine, 4 who converted to general anesthesia, and 1 with incomplete records, the final analysis included 74 participants. The control group, which consisted of non-infected parturients, included 81 parturients from January 2017 to December 2021. After excluding 15 parturients who converted to general anesthesia and 1 with incomplete records, 63 participants were included in the final analysis. A total of 137 patients were included in the analysis.

Age, BMI, gestational weeks, urgency, site of puncture, approach of puncture, operation time, block-incision time, Apgar scores at 1 and 5 min, and newborn body weight showed no significant differences between the two groups (Table 1). However, the duration of the hospital stay was longer in the COVID-19 group than that in the control group.

The perioperative anesthetic variables are described in Table 2. There were no significant differences between the two groups in sensory block height, base mean blood pressure, lowest systolic blood pressure after spinal anesthesia, total phenylephrine dose, total ephedrine dose, or total infused crystalloids. However, the bupivacaine dose was lower in the COVID-19 group than that in the control group. The baseline SpO₂ was higher in the COVID-19 group than that in the control group. The BHR was higher in the COVID-19 group than that in the control group, whereas the base systolic blood pressure was lower. The total infused colloid concentration was higher in the COVID-19 group than that in the control group.

In both groups, there were no significant correlations between BHR and the variables listed in Table 2 (phenylephrine, ephedrine, colloid, crystalloid usage, lowest SBP after block, days from COVID-19 diagnosis to surgery, etc.). However, there was a weak positive correlation between BHR and the length of hospital stay in the COVID-19 group ($P = 0.000$, Spearman's rho = 0.422).

Subgroup analysis

In the COVID-19 group, patients were divided into sub-

groups based on BHR: those with a BHR of 100 or higher (group H) and those with a BHR below 100 (group L) (Table 3). There were no significant differences between the two groups in terms of Apgar score at 5 min or newborn body weight. However, the duration of postoperative hospital stay was longer, and the Apgar score at 1 min was lower in group H than that in group L.

Table 1. Baseline Characteristics of the COVID-19 and Control Groups

Variable	COVID-19 (n = 74)	Control (n = 63)
Age (yr)	34 (32, 37.3)	34 (31, 36)
Body mass index (kg/m ²)	25.9 (24.8, 28.1)	26.7 (25.2, 28.8)
Gestational weeks	38 ± 1.4	38.1 ± 1.3
Urgency		
Elective	56	15
Emergency	18	13
Site of puncture		
L 4-5	72	59
L 3-4	2	4
Approach of puncture		
Median	70	60
Paramedian	4	3
Operation time (min)	64 (53.8, 76)	61 (55, 71)
Duration of hospital stay (d)	6 (4, 7.3)	4 (4, 4)
Block-incision time (min)	15 (12, 18)	15 (10, 17)
Apgar score 1 min	9 (8, 9)	9 (8, 9)
Apgar score 5 min	9 (9, 10)	9 (9, 10)
Newborn bodyweight (kg)	3.2 ± 0.4	3.3 ± 0.4

Values are presented as median (1Q, 3Q), mean ± SD, or number only. $P < 0.05$.

When comparing the severity of COVID-19 respiratory symptoms before surgery in group H, the distribution was as follows: none, 36.4% (8 parturients); mild, 59.1% (13 parturients); and moderate, 4.5% (1 parturient). In Group L, the distribution was none 48.1% ($n = 25$), mild 46.2% (24), and moderate 5.8% (3). There was no significant difference between the two groups ($P = 0.315$).

Additionally, the proportion of patients experiencing worsening COVID-19 symptoms after surgery was higher in group H (31.8%) than that in group L (13.5%). In group H, 18.2% of the patients (4 parturients) were transferred to the respiratory department due to increased oxygen demand, and 13.6% (3 parturients) had increased CRP and procalcitonin levels. In contrast, in group L, 9.6% (5 parturients) were transferred to the respiratory department because of increased oxygen demand, and 3.8% (2 parturients) had increased CRP and procalcitonin levels.

In group H, a positive correlation was observed between the BHR and the lowest SBP after the block ($P = 0.012$, Spearman's $\rho = 0.528$).

DISCUSSION

The study did not observe any significant differences in the occurrence or vasopressor usage when comparing the COVID-19 group to the control group. Despite the lower amount of bupivacaine used and the higher usage of colloids in the COVID-19 group, it is difficult to attribute these differences to clinical significance. However, it was observed that the higher the patient's heart rate before anesthesia, the more severe the hypotension after spinal anesthesia. One of

Table 2. Perioperative Anesthetic Variables

Variable	COVID-19 (n = 74)	Control (n = 63)
Bupivacaine dose (mg)	7 (7, 8)*	8 (7.5, 8)
Sensory block height	T6 (T6, T10)	T6 (T6, T8)
Base SpO ₂ (%)	100 (99, 100)*	99 (98, 100)
Base Heart Rate (bpm)	89 (78.8, 102.3)*	79 (73, 94)
Base mean blood pressure (mmHg)	95.5 (88.6, 108)	100 (91, 108)
Base systolic blood pressure (mmHg)	121 (112, 130)*	129 (123, 141)
Lowest systolic blood pressure after spinal anesthesia (mmHg)	88 (82, 96.5)	87 (81, 100)
Total phenylephrine dose (mg)	0.3 (0.1, 0.5)	0.2 (1, 0.4)
Total ephedrine dose (mg)	0 (0, 5)	0 (0, 5)
Total infused crystalloid (ml)	500 (500, 500)	500 (400, 800)
Total infused colloid (ml)	500 (500, 1,000)	500 (500, 500)

Values are presented as median (1Q, 3Q). * $P < 0.05$.

Table 3. Subgroup Analysis of the COVID-19 Group Based on Baseline Heart Rate

Variable	Heart rate $\geq$ 100 (n = 22)	Heart rate < 100 (n = 52)
Duration of hospital stay (d)	7 (5, 9)*	5 (4, 6.8)
Apgar score 1 min	8 (8, 9)*	9 (8, 9)
Apgar score 5 min	9 (9, 9)	9 (9, 10)
Newborn bodyweight (kg)	3.2 $\pm$ 0.4	3.1 $\pm$ 0.4
Worsening of COVID-19 symptoms after surgery	7 (31.8)*	7 (13.5)

Values are presented as median (1Q, 3Q), mean $\pm$ SD, or number (%). Worsening COVID-19 symptoms: increased oxygen demand and C-reactive protein and procalcitonin levels. *P < 0.05.

the significant findings of this study was that it revealed a correlation between an increased heart rate and worsening COVID-19 symptoms.

COVID-19 in pregnant women is associated with various risks, such as preeclampsia and preterm birth [9,10]. Spinal anesthesia is recommended when performing cesarean section in such cases [11-13]. During anesthesia for patients with COVID-19, anesthesiologists wear Level C protective equipment. This limits visibility and mobility, thus increasing the risk of contamination of procedural tools or sites. Therefore, spinal anesthesia is recommended to mitigate these risks. This recommendation is based not only on the proven safety of spinal anesthesia but also on its potential to minimize the risk of infection for medical staff. Despite the recommendation for spinal anesthesia, hypotension is frequently observed during such procedures, prompting our study to investigate and confirm these occurrences. This study is noteworthy, as it is the first study to investigate the factors associated with the occurrence of hypotension during spinal anesthesia for cesarean section in parturients infected with COVID-19 in Korea.

The hospitalization period was longer in the COVID-19 group than that in the control group. This difference in hospitalization periods is likely attributable to the fact that at the time of the study, the basic isolation period for COVID-19 release in South Korea was 1 week.

The reason why the incidence of low blood pressure was not high in the COVID-19 group seems to be the use of bupivacaine, vasopressors, and intravenous fluids without clear standards and the lack of unified timing for their administration. This environment featured stronger monitoring than regular parturients, and there may have been greater use of prophylactic vasopressors in the COVID-19 group than that in the control group.

Among the studies published to date, one reported similar rates of hypotension following a neuraxial block in both par-

turients with COVID-19 and those without [7], whereas another reported a lower occurrence of hypotension in parturients with COVID-19 [8]. In particular, Scoon's study [8] can be juxtaposed with ours as it exclusively focused on patients undergoing spinal anesthesia, administering vasoconstrictors prophylactically via bolus or injection post-spinal anesthesia. Future studies should consider the timing of vasopressor administration as a critical factor.

In the subgroup analysis, there was a statistically significant difference in the Apgar scores between the group with a BHR of 100 or higher (group H) and the group with a BHR below 100 (group L) in parturients with COVID-19. Moreover, there were more cases of clinical worsening of COVID-19 symptoms in Group H than those in Group L (32% vs. 14%, respectively). Considering this, it can be speculated that the prolonged hospitalization period in patients with COVID-19 may be attributed to the worsening of symptoms. In conclusion, a high BHR in parturients with COVID-19 before cesarean section was correlated with an increased length of hospital stay.

Furthermore, in group H, parturients with higher BHR showed a more pronounced decrease in blood pressure after spinal anesthesia. This indicates that when administering spinal anesthesia to parturients with a BHR of 100 or higher, it is important to be aware that there may be a more significant drop in blood pressure after spinal anesthesia.

Although the exact reasons for the increase in BHR in parturients with COVID-19 require further investigation based on clinical experience, it is speculated that increased anxiety due to the unfamiliar environment and fear of COVID-19 infection might play a significant role. Anxiety tends to increase in patients with COVID-19, potentially leading to an elevated heart rate [14].

Our study has some limitations. In the case of parturients with COVID-19, there were instances in which patients entered the operating room with oxygen administered through

a nasal cannula, depending on their symptoms. However, this information is not consistently documented in medical records, leading to potential errors. Owing to the nature of retrospective studies, we could not apply a standardized protocol for hypotension prevention and treatment, such as fluid management and vasopressor use.

In conclusion, our study found no evidence to suggest that parturients with COVID-19 undergoing cesarean section under spinal anesthesia experienced higher rates of hypotension than non-infected parturients. However, within the COVID-19 group, those with a higher BHR tended to experience a more significant blood pressure reduction.

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None.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

Writing - original draft: Si Ra Bang, Sung Jun Cho. Writing - review & editing: Gunn Hee Kim, Mi Jung Yoon. Conceptualization: Gunn Hee Kim, Mi Jung Yoon. Data curation: Sung Jun Cho. Formal analysis: Si Ra Bang. Methodology: Gunn Hee Kim, Mi Jung Yoon. Project administration: Si Ra Bang. Supervision: Gunn Hee Kim. Validation: Mi Jung Yoon.

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